Lab 7A • 05/07/12

D versus L configuration of carbohydrates

This is the simplest one, d-glyceraldehyde. That d designation was both arbitrary and a guess. In the 1860s, 70s, and 80s, when the idea of tetrahedral carbon came about, they made this realization that if you had a formula just like this, you're going to have this thing called a stereocenter. What is the difference or similarity in physical properties between enantiomers? Which physical properties are same an which ones are different? Only optical rotation; every other physical property is exactly the same. If you were a researcher in the 1870s, 1880s, and you didn't have all the techniques that we have now, how would you know that whichever form caused a positive rotation was also the R form? When we make R and S designations, it has nothing to do physically with the molecule; it's just our system saying: you're more important that you, but not on a chemical basis, just on the basis of atomic numbers, for example. There is no physical relationship between something being R and which way it rotates light; the only relationship that's there is that if the R form twists light one way, the S form twists light the opposite way. You can have compounds that are R configuration but have a positive effect on rotation, and you could have ones that are R and a negative effect.

Fischer was faced with this dilemma. He knew that there were two sugars that we could call glyceraldehyde, that there were two sugars that would be mirror images and identical in every possible way except optical rotation, so he picked one and called it the d form, corresponding to a positive rotation. It was a guess, a total guess. Why does that matter? You can make other compounds easily from glyceraldehyde. Let's say that we had the full set of modern synthesis tools. We could reduce that aldehyde; we could oxidize it to a carboxylic, that would be a related molecule, still with that same stereoconfiguration. Even more importantly, we can build all of the other sugars from glyceraldehyde. For example, what would happen if we reacted glyceraldehyde with hydrogen cyanide? What happens with a carbonyl compound reacting with hydrogen cyanide? A cyanohydrin. What happens – a cyanohydrin means having an -OH group next door to a cyano group or, what in organic terms, we call a nitrile. Once I do react the carbonyl, I've made a new stereocenter; that's why I've drawn it with wiggly lines. The geometry of the carbonyl is planar, it's an sp2-hybridized center; that means that attack from above or below is, in principle, equally likely. That means that that -OH group, the one with the wiggly line, has a 50/50 chance, presumedly, of being on the left or the right, so you make two new sugars by doing this process. Then, you're left with a nitrile up top. Nitriles can be reduced to amines, but just in the same way that carbon-carbon triple bonds can be selectively reduced to a carbon-carbon double bond by using a poisoned catalyst, same thing can happen here. If we did only reduce down to the double bond, what kind of functional group do I now have, at least on that carbon there? An imine. What if I hydrolyze an imine, what do I get? A carbonyl, again an aldehyde. That means I've made a carbohydrate again, so I took one sugar and did what's called chain extension – made another sterocenter, but notice that the bottom stereocenter never got affected. The point here is that all naturally-occurring sugars have mirror image forms; between mirror images, the only difference is optical rotation. That means that, no matter how many stereocenters are on the sugar, half of those sugars are just mirror images of the other half.

So, to classify them, since the simplest sugar has that one stereocenter that, by extension never gets touched, then all sugars are classified according to that last stereocenter's configuration. Since, arbitrarily, d-glyceraldehyde was called the d for, then when that -OH group on the bottom sterocenter is on the righthand stereocenter is on the righthand side for that last stereocenter, that's what makes a sugar a d sugar. If I circle that motif in each of these, you can see that they all have that same configuration. Carbohydrates are classified as d or l on the basis of the configuration of the stereocenter that is furthest from the anomeric position. If I were to show you for glucose, on the righthand side, if you look at the substituents there, if you can remember right-left-right-right, that is the correct pattern for substituents on glucose – that is, if we're talking about d glucose, because that last stereocenter on the penultimate carbon, it's on the righthand side. Enantiomers are non-superimposable mirror images, which means every group that's S on one molecule is R on the other, and every group that's Ron one molecule is S on the other – in other words, all the stereocenters are inverted between one enantiomer and another. When we say non-superimposable mirror images, we do have to remember, though, that they're stereoisomers, which means they have exactly the same connectivity, it's only this difference in the 3D arrangement that's going on here. Enantiomers are stereoisomers that are mirror images but non-identical; in other words, they're not superimposable. One way to make an enantiomer is to remember that all stereocenters are inverted.

That's key to keep in mind, because we have this d form of glucose that I want to make into the l form. The l form is determined by the configuration of the bottom stereocenter, but to go from the d form to the l form, we don't just flip the bottom one; enantiomers mean that all stereocenters are inverted. That means the l form of glucose is going to look like this, where the -OH groups are left-right-left-left, instead. [The d and l configuration] is [based] on what the last stereocenter is doing. Notice that's based on keeping the carbonyl on top and calling that end of the molecule the beginning of the molecule.

What are diastereomers? Non-identical non-mirror-image stereoisomers. They have the same connectivity, same atoms hooked up to each other, but they are not mirror images, and they still differ in their 3D positions. Only some, not all, stereocenters are inverted. Diastereomer is a broad category. Within that, we have a sub-category of epimers. What are epimers? Stereoisomers in which only stereocenter is different between them.

This means you have to have more than one stereocenter, because if you only had one and you flipped it, that's an enantiomer. [A diastereomer has to have] more than one stereocenter, two or more. In those cases, only one of them changes from one diastereomer to the other, if we're talking about epimers. Epimers are diastereomers that differ in the configuration of only one stereocenter.

Now we're going to learn a sub-class of that: anomers, which are epimers that only occur in carbohydrates.

For six-carbon sugars, six carbons, the top one and the bottom one are not stereocenters, cause the top is a carbonyl, the bottom is CH2OH; if you have two hydrogens, that means it's not a stereocenter. There's four stereocenters, but one of them is that d/l center, so we'll ignore that, because for half of the sugars, it's one way, for their mirror images, it's the other. That means that the sugars themselves only differ on the basis of three stereocenters. Two to the third [power] is 8, so there's 8 sugars you need to know. These are all going to be the d sugars, so the last stereocenter on each one has the -OH group on the righthand side. Let me fill the rest of these in, then I'll explain the pattern that's going on. [riff about binary numbers] In decimal, we count 0, 1, 2, 3, 4, 5, 6, 7, 8, 9; we run out of numbers, so what do we do? We move over to the next digit; that's called the 10's place because that's why we had to move over there. Then, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19; ran out of numbers again, so then we go 20. Octal – eight: we go 0, 1, 2, 3, 4, 5, 6, 7, 10, 11, 12, 13, 14, 15, 16, 17, 20, 21, 22, 23, 24, 25, 26. The highest number you can get up to is 77, and then you jump to 100, cause you only count from zero through seven, which eight numbers, which is three binary digits. In binary, you can only count zero or one, so number 0, then you add 1, you're at the number 1. You run out of numbers, so when you add another one, you turn into the number 10. [There are only 10 kinds of people in the world]

What's the point of this? Look at these sugars. If I call the righthand side zero and the lefthand side one, then notice that the first sugar, I have [0000] (my digits are read from bottom to top). In other words, if I turn my head and look this way and read from left to right [0000], [0001], [0010], [0011], [0100], [0101], [0110], [0111] – binary numbers 0 through 7. Why in the world am I showing you this? I don't have to memorize these structures; I just memorize the names, cause I just remember, write out 0 through 7 in binary, I'll get all the structures. Then, if you can memorize: allose, altrose, glucose, mannose, gulose, idose, galactose, talose – then you've got all eight sugars memorized. That's if you can remember this binary trick. These are just the hexoses, those sugars with six carbons. There's five-carbon ones: there's ribose, arabinose, xylose, and lyxose. There's four-carbons: erythrose and threose; and then there's the three-carbon: glyceraldehyde.

Let me show you what this anomer thing is. d-Glucose. Observe that, if I start at the carbonyl and count the carbon in the carbonyl as position one and go to the sixth position (five atoms away) – I can choose oxygen to be that sixth position, which anticipates the fact that that -OH group can react with the carbonyl. What kind of functional group would be formed if that -OH reacted with the carbonyl? [A hemiacetal]. Why don't we walk through the mechanism. The bottom four stereocenters don't get affected by any of this; the top is currently sp2-hybridized because it's a carbocation, so in principle, at the moment, it doesn't matter how I write it. The next step is going to be attack-deprotonate. What's going to happen to the stereochemistry of what used to be the carbonyl, once I actually close the ring? Aren't there two ways this can close up? If, for example, the carbocation is such that molecule's in the plane of the paper, that means that the p-orbital is pointed towards you or away from you. That means that when this thing loops around to make a ring, it can attack onto the front part of that p orbital, or it could attack on the back. If we ignore any steric considerations, both of those are 50/50 equal[ly] likely in probability, aren't they? That means when we close the ring, we make two compounds, but they're from the same starting material, so they're the same sugar. But if there's the possibility of forming one stereocenter or another, we've just made epimers that don't exist when the molecule is linear. That's what anomers are – anomers are epimers that occur in carbohydrates only when they cyclize and create a new stereocenter from what used to be a carbonyl. How do we write one of these, and how do we name which one of these anomers it is?

First, let's finish the mechanism. I now have five rungs on my ladder, five arms off my backbone, cause I made a new stereocenter. Everything that's on the bottom still has the same configuration: right, left, right, right. The top one – whether in real life you have exactly 50/50 distribution of if it's slightly off, you're still going to have both stereochemical possibilities. In one of these, the -OH group will be on the right; in one of these, the -OH group will be on the left. Unfortunately, we stil have a proton on that bottom oxygen, so we need to go through a deprotonate step.

What looks odd about this molecule? It's in a ring form, but, remember what the strict definition of Fischer projection space is – we want to imagine, ideally, a compound as if it's on a tube, and we're just scrolling along the backbone of that. But, the way I've got it drawn currently, it's like the ring comes around and it goes sticking off to the side suddenly. In order to be able to properly visualize this as a true ring, we need to rewrite this Fischer projection. What I'm saying we want is for the ring to be just in the backbone, instead of coming off to the side. We learned before that if we take any two groups and swap them twice, or if we take three groups and rotate them, then you maintain the configuration of the stereocenter. I'm going to take just one form [anomer] to do the rest of this with; I'm going to choose the one on the left, and I'm going to precess the groups. That will not change the configuration of the stereocenter. If we compare the leftover group that was at that bottom stereocenter, and the new -OH group we made up top.

Anomeric position. In acyclic sugars, there is a carbonyl which is not a stereocenter that, once this sugar is cyclized, becomes a tetrahedral center and therefore becomes a stereocenter – that is the anomer position. In acyclic sugars, the carbonyl carbon is not a stereocenter. Once cyclization occurs, that carbon adopts a tetrahedral geometry, so it becomes a stereocenter. Since that stereocenter, in principle, has a 50/50 chance of being one configuration or the other – even if it's not 50/50, it's still going to have the two possibilites – then that's why we have epimers that only form at this point. When you end up with the epimer so that the new -OH group is trans across the ring, when properly drawn, from this lower group, this is the alpha form. I say trans when properly drawn, cause look at the structure we had originally – that CH2OH group was neither to the left or the right, so we couldn't correctly interpret whether it was cis or trans. We had to make the ring fully in the backbone so we could project and see this properly as now being trans. The other one, if you drew it out, it is the beta form, because once you do rewrite it, you'll see that the new -OH group and that CH2OH group are on the same side of the ring.

[We need] to convert this into its proper cyclic projection form. Although [I've said] you can turn [Fischer projections] 90°, we're going to turn this 90° – because we're not making it a Fischer projection any more, we're going to change the way we're drawing exactly this structure. What this means to us is we have a series of hydrogens and -OH groups across bars, where those bars are up and down, with the ring itself puckered out at you; the rest of the ring is just back behind us. We're actually looking at it at this perspective for the moment, because remember that in a Fischer projection, it's supposed to be that everything that's up and down is pointed away from us, so notice that the top and bottom of my arms are pointed away from you. Then we have all of these cross bars. I'm going to take this structure and ignore the fact that it's a Fischer projection and just flop it 90° and then take all of those rungs and distribute them out evenly along the ring. Let's see what that looks like. First, improper rotation. I keep all of the groups in the same order, so we still pretend that what's in front here really, truly is in front, because that's the way it was just one step before. The oxygen, whether I wrote it on the right or the left, it doesn't matter, it's a ring. What was on the left on the Fischer projection is now going to be on the top of this new structure. We do one last step: instead of a ring, we make a hexagon, in this case because it's a six-membered ring. We still write the same groups in the same order. This is what's called a Haworth projection. By convention, the anomer position is placed at the very right of the ring. This is used for visualization purposes.

Di- and trisaccharides are compounds where you take these single sugar units – usually five or six carbons – and combine them together. When we combine them, almost always it's one or both sugars becoming cyclic in form, so we need to be able to draw it this way in order to be able to draw the connection between one sugar to the next.

The full name of this compound: this is alpha – why alpha? Because these squared groups are trans to each other. alpha-d-glucopyranose. What does pyranose mean? From pyran, which is six-membered ring with two double bonds, but also with the oxygen in the ring, just like this. Pyranose, by extension, means a six-membered ring with an oxygen in it. Furan, same thing that THF comes from, tetrahydrofuran, that's a five-membered ring. When I was cyclizing the compound, what if I took the -OH group from the third stereocenter instead of the fourth? I would have made a five-membered ring, and that would have been the furanose form. When I make the six-membered ring, there's an alpha and beta form; when I make the five-membered ring, there's an alpha and beta form. And, of course, there's the l-sugar. If you just say glucose, there's eight forms when it's in its cyclic form – alpha-l-glucofuranose, alpha-l-glucopyranose, alpha-d-glucofuranose, alpha-d-glucopyranose, beta-l-glucofuranose, beta-l-glucopyranose, beta-d-glucofuranose, beta-d-glucopyranose.

[lab directions]

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d-glyceraldehyde

Carbohydrates are classified as D or L on the basis of the configuration of the stereocenter that is furthest from the anomeric position.

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epimers – diastereomers that differ in the configuration of only on stereocenter.
anomers – epimers that only occur in carbohydrates

anomeric carbon/anomer position – in acylic (linera) sugars, the carbonyl carbon is not a stereocenter; once cyclization occurs, that adopts a tetrahedral geometry, so it becomes a stereocenter

Haworth projection

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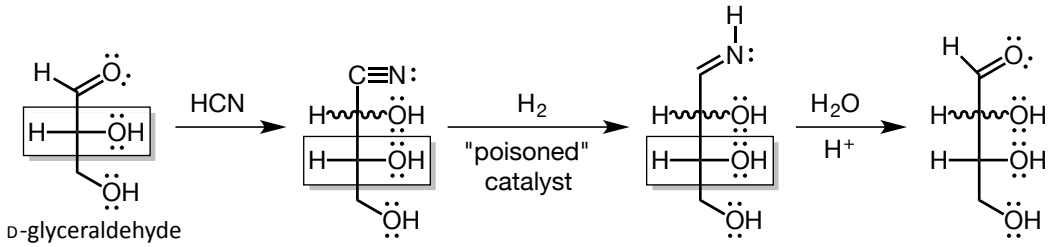
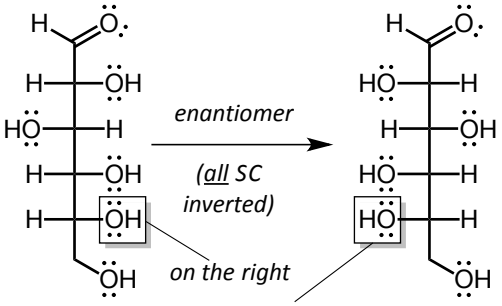


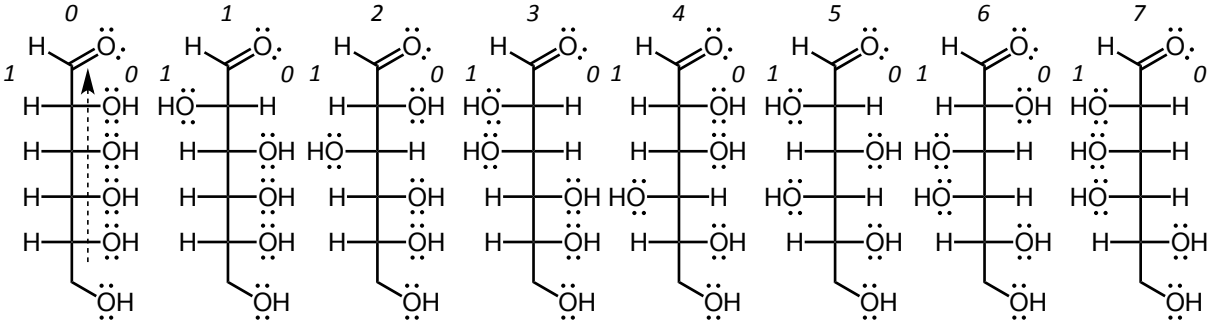
D-glyceraldehyde

05/07/12 lab • 2

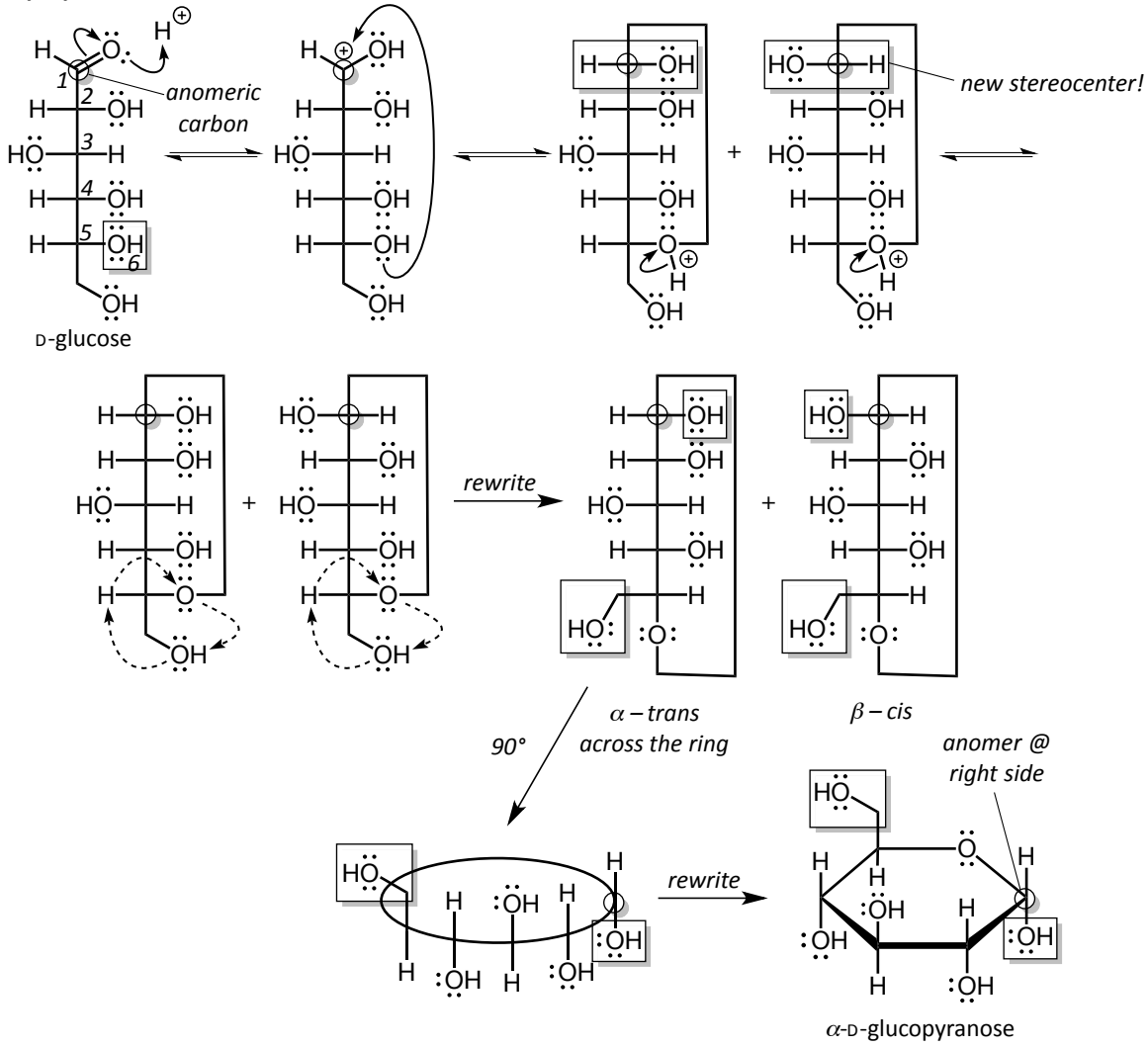


D-glucose L-glucose

05/07/12 lab • 3



D-allose *0000* | D-altrose *0001* | D-glucose *0010* | D-mannose *0011* | D-gulose *0100* | D-idose *0101* | D-galactose *0110* | D-talose *0111*


anomeric carbon
new stereocenter!
D-glucose
rewrite
+
α – trans across the ring
β – cis
90°
anomer @ right side
rewrite
α-D-glucopyranose